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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,410	08/04/2003	Stevan P. Tofovic	007278-10	6070

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
12/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/633,410	**Applicant(s)** TOFOVIC ET AL.	
	Examiner Renee Claytor	**Art Unit** 1617	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 November 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See continuation sheet
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s).
13. ☐ Other: _____.

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

Applicants arguments over the 35 USC 112, first paragraph rejection have been fully considered and are not found persuasive. Applicants argue that it is for the FDA and not the USPTO to decide when a drug is efficacious or not. The issue at hand is not whether the drug is efficacious. The Examiner has stated that there is enablement for the treatment of nephropathies, suggesting that it is recognized that there is a use for the drug. However, there is no sufficient data in the specification showing how to prevent nephropathy from ever occurring. Applicants have specifically pointed to paragraphs 0055, 0058, 0059 and 0060 in support of their argument that 2-OHE can treat and prevent disease. In response to the assertions, to prevent something means to keep from ever occurring; therefore, prevention of a disease is an absolute term. It is reiterated that the specification teaches that administration of 2-OHE reduced PAN-induced mortality by 66%. This shows that some mortality still occurred and the disease was not prevented. It is further shown that 2-OHE significantly reduced the labeling index of glomerular immunoreactive PCNA in PAN-treated animals, reduced the number of inflammatory cells in glomeruli and in the interstitium in PAN-treated animals and significantly decreased PAN-induced increases in collagen IV and the labeling index of glomerular immunoreactive collagen IV in PAN-treated animals. Accordingly, treatment with 2-OHE shows decreases in various markers for kidney disease, but does not show total prevention of the disease from every occurring.
Applicants arguments over the 35 USC 103 rejection in view of Tofovic have been fully considered. Applicants assert that Tofovic does not teach that the conditions being treated are drug-induced nor teaches the prevention of such drug-induced conditions and also assert that there is no suggestion to modify the teachings in order to prevent the conditions mentioned or that the teaching would be effective in treating or preventing drug-induced conditions. In response to the arguments about prevention, see the above arguments in the 35 USC 112 rejection. Further, the Examiner will point out that all of the conditions are associated with nephropathies regardless of how they originated; therefore, it is obvious that the teachings of Tofovic et al. would necessarily treat nephropathies regardless of it is drug-induced or naturally occurring. Further, Applicants make arguments to relate the rejection of the 35 USC 112 rejection teaching that prevention is an unpredictably and undeveloped art. In response, the statement made in the 35 USC 112 rejection were addressing the claim limitation of "prevention" and not the case of treating nephropathies as a whole. In response to the arguments against the Xiao et al. reference that 2-OHE does not induce NO synthesis and does not protect against renal disease and because of this there is no reasonable expectation of success. As pointed out in the previous Office Action, Xiao et al. teaches that the metabolites of estradiol, including 2-OHE, are effective at inhibiting GMC growth by inhibiting DNA synthesis, collagen synthesis and cell proliferation (second paragraph, Figures 4 and 5) and the authors conclude that the metabolites may prevent glomerulosclerosis by the inhibition of abnormal growth of GMC's. Even though the metabolites are acting via a different mechanism, they are still effective in inhibiting growth of GMC's. The arguments against Tofovic et al. and Xiao et al. in view of Allison are that the rejection is not valid because Tofovic et al. and Xiao et al. do not teach each and every element of the claims. Those arguments have been addressed above and the rejections are maintained.